

## Therapeutic, Ethnomedicinal and Pharmacological Perspective of Bitter Apple Fruit (*Citrullus Colocynthis* (L.) Schrad

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**Abstract:** *Citrullus colocynthis* (L.) Schrad is a valuable cucurbit plant, widely distributed in the desert areas of the world. *Citrullus colocynthis* fruits are usually recognized for its wide range of medicinal uses as well as pharmaceutical and nutraceutical potential. The plant has been reported to possess a wide range of traditional medicinal uses including in diabetes, leprosy, common cold, cough, asthma, bronchitis, jaundice, joint pain, cancer, toothache, wound, mastitis, and in gastrointestinal disorders such as indigestion, constipation, dysentery, gastroenteritis, colic pain and different microbial infections. Several bioactive chemical constituents from fruits were recorded, such as, glycosides, flavonoids, alkaloids, fatty acids and essential oils. The isolation and identification of cucurbitacins A, B, C, D, E, I, J, K, and L and Colocynthosides A, and B were also reported. The fruit of *Citrullus colocynthis* has been studied extensively for its wide range of biological activities, which include antioxidant, cytotoxic, antidiabetic, antilipidemic, insecticide, antimicrobial and anti-inflammatory. The plant was also shown to be rich in nutritional value with high protein contents and important minerals as well as edible quality of seed oil. It is evident from the literature that *Citrullus colocynthis* possesses a wide range of medicinal uses and has been well studied for its antidiabetic, anticancer, antioxidant, antimicrobial and anti-inflammatory activities, while its therapeutic potential for gut, airways and cardiovascular disorders remains to be explored. Critical analysis revealed that the plant has the huge potential for pharmaceutical and nutraceutical application, with some indications for the presence of synergistic and /or side effects neutralizing combinations of activities.

**Key words:** *Citrullus colocynthis* (L.) Schrad, pharmacological, ethnomedicinal, therapeutic, cucurbitacins, nutraceutical.

## Introduction

Health consciousness and increased knowledge about the side effects of synthetic drugs have enhanced interest in traditional medicines. Medicinal plants offer cures for various diseases, leading to improved living standards.[1,2] This has brought ethnomedicinal studies into the spotlight and increased demand for herb-based medicines. *Citrullus colocynthis* is an herbaceous plant containing an abundance of nutrients that play a key role in the improvement of wellbeing. *C. colocynthis* has many biological properties, such as antioxidative, hypoglycemic, antibacterial, anti-cancerous, anti-inflammatory, analgesic, gastrointestinal tract, reproduction, protection, anti-microbial, antidiabetic, hypolipidemic, antineoplastic, profibrinolytic, anti-allergic, pesticidal, and immune-stimulatory. There are numerous bioactive compounds like cucurbitacin, flavonoids, and polyphenols in *C. colocynthis* that give it medicinal properties. Scientific literature evidenced that owing to the bioactive constituents, including cucurbitacin, polyphenols, flavonoids, and other potent molecules, *C. colocynthis* has many pharmacological and physiological functions. It possesses multi-beneficial applications in treating various disorders of humans and animals. So, the primary purpose of this comprehensive review is to provide an overview of the findings of positive impacts and risks of *C. colocynthis* consumption on human health, especially in poultry and veterinary fields.

*Citrullus colocynthis* is a desert plant and a source of several bioactive compounds such as essential oils, glycosides, flavonoids, alkaloids, and fatty acids. Medicinal plants improve the immune system. The dried fruit pulp of *C. colocynthis* has been used to treat gastrointestinal disorders like indigestion, gastroenteritis, and intestinal parasites. *C. colocynthis* also has excellent pharmacological properties, such as being a laxative and purgative; it is anti-diabetic, anti-inflammatory, anthelmintic, and anti-cancerous. The fruit has been studied extensively for its antimicrobial, antioxidant, and anti-inflammatory activities. *C. colocynthis* has antidiabetic, hypolipidemic, antineoplastic, profibrinolytic, antiallergic, antimicrobial, pesticidal, and immune-stimulatory effects. It also affects the reproductive system and fertility [3,4]. Many other products have been selected as alternatives to antibiotic growth promoters; these include probiotics, prebiotics, enzymes, organic acids, acidifiers, antioxidants, and phytogenic additives.

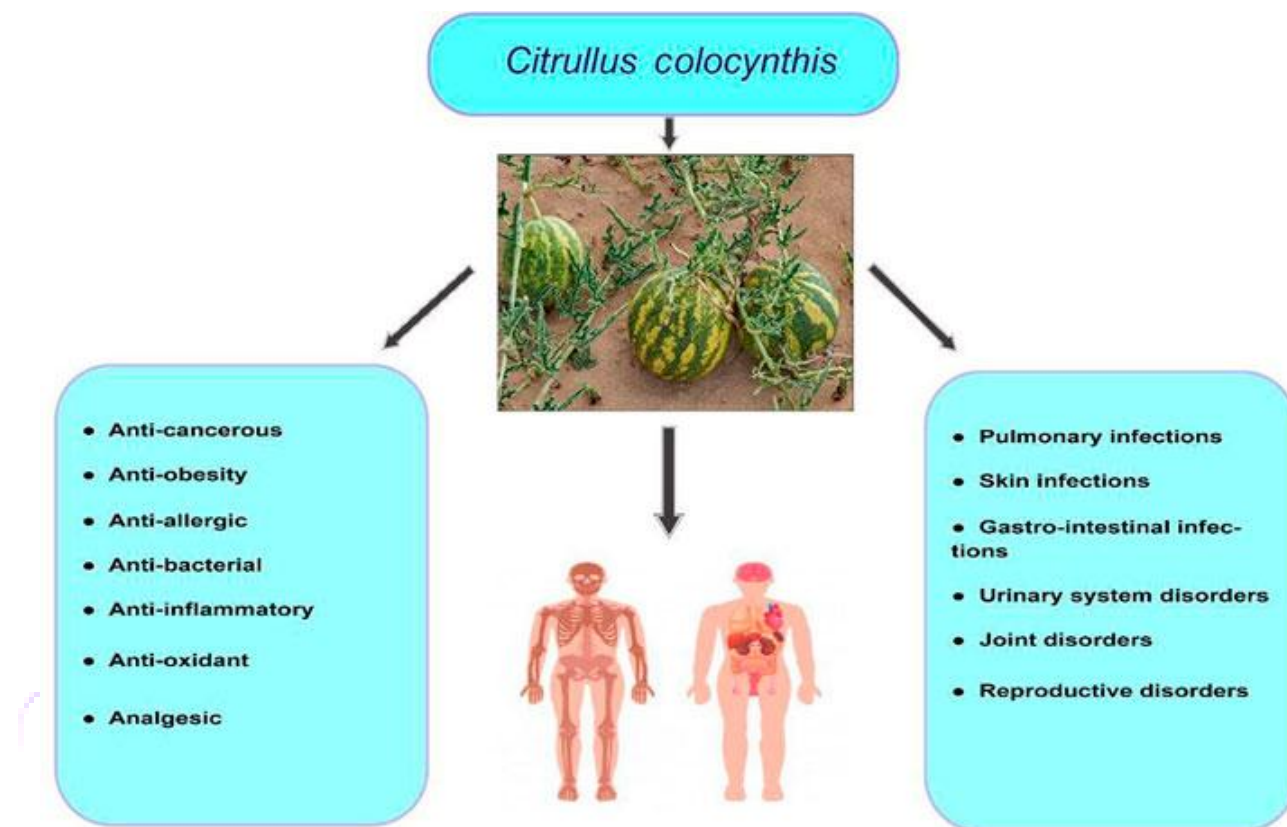
*C. colocynthis* is a perennial plant with perennial roots and angular, tough, rough, and vine-like stems that spread on the ground and may climb up from there. They produce a single yellow flower at leaf axils. They are monoecious and have long peduncles and tuberous rootstock sprouting long trailing or climbing stems



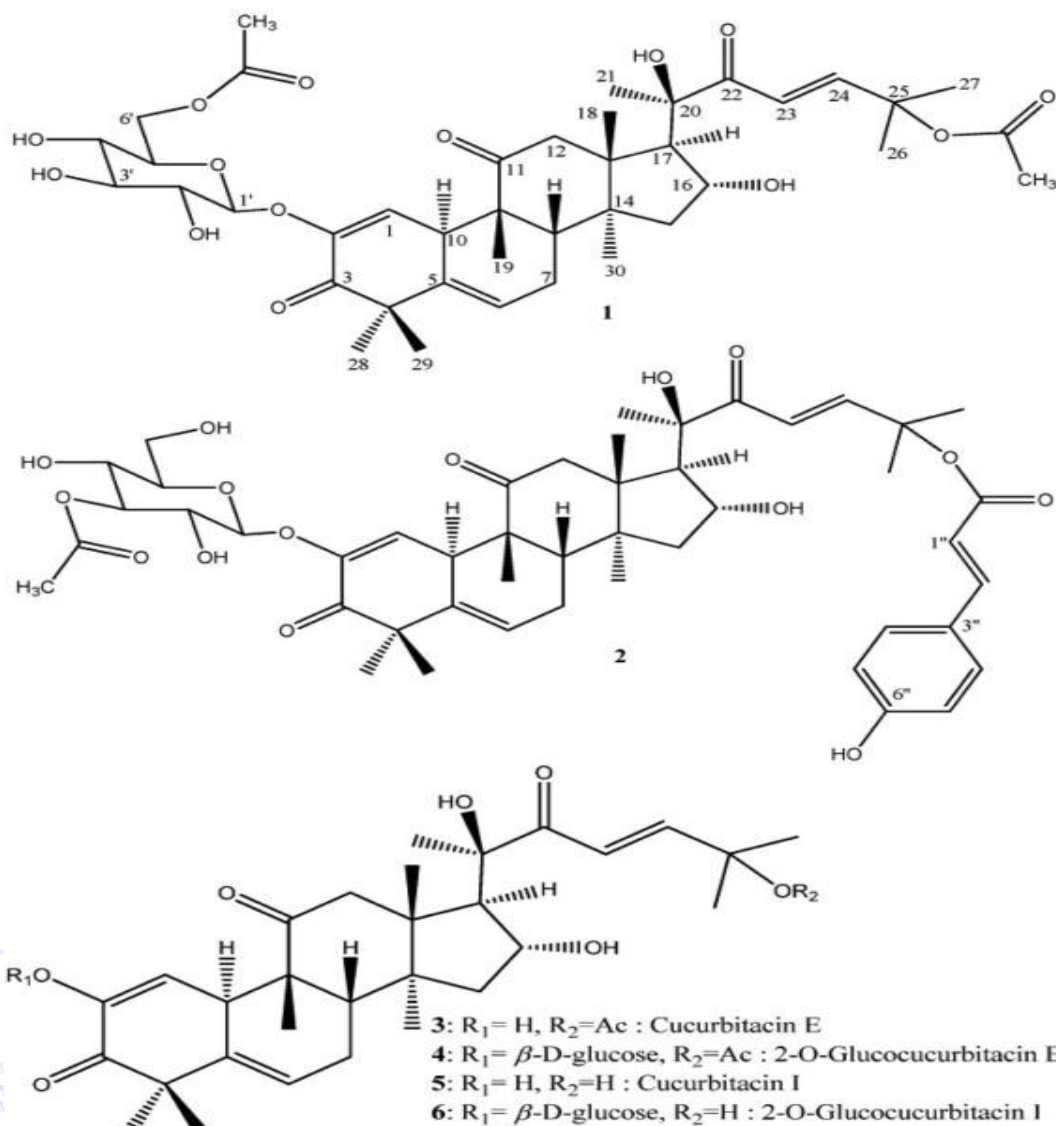
(A) Seeds (B) roots (C) plant (D) leaf (E) flower and (F) fruit of *C. colocynthis*

## Discussion

*Citrullus colocynthis* is used widely in different parts of the world for the treatment of a number of diseases including diabetes, constipation, leprosy, asthma, bronchitis, jaundice, joint pain, cancer and mastitis.

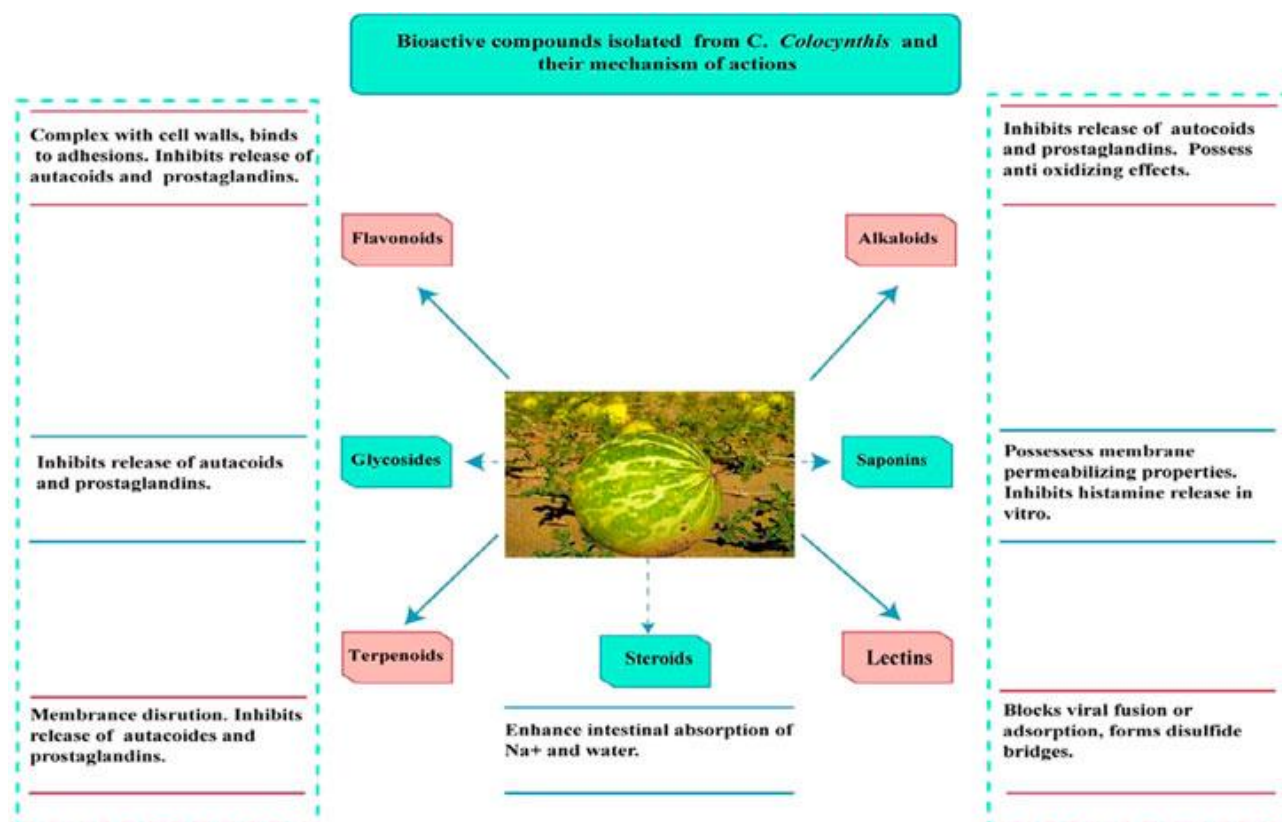


Several bioactive compounds of *Citrullus colocynthis* fruit have been recorded in the literature. They are grouped as glycosides, flavonoids, alkaloids, carbohydrates, fatty acids, and essential oils. The traditional medicinal applications of *Citrullus colocynthis* have inspired many pharmacological investigations. Several extracts and isolated compounds have been evaluated for their biological activities, especially anticancer and antidiabetic activities. There seems to be an interest in developing new anticancer/antitumor drugs from *Citrullus colocynthis* due to its high contents of cucurbitacins. The plant roots are large, fleshy, and perennial, leading to a high survival rate due to the long tap root. [5,6] The vine-like stems spread in all directions for a few meters looking for something over which to climb. If present, shrubs and herbs are preferred and climbed by means of auxiliary branching tendrils. Very similar to watermelon, the leaves are palmate and angular with three to seven divided lobes. The flowers are yellow and solitary in the axes of leaves and are borne by yellow-greenish peduncles. Each has a subcampanulate five-lobed corolla and a five-parted calyx. They are monoecious, so the male (stamens) and the female reproductive parts (pistils and ovary) are borne in different flowers on the same plant. The male flowers' calyx is shorter than the corolla. They have five stamens, four of which are coupled and one is single with monadelphous anther. The female flowers have three staminoids and a three-carpel ovary. The two sexes are distinguishable by observing the globular and hairy inferior ovary of the female flowers. The fruit is smooth, spheric with a diameter of 5 to 10 centimetres (2 to 4 inches) and an extremely bitter taste. The calyx englobe the yellow-green fruit which becomes marble (yellow stripes) at maturity. The mesocarp is filled with a soft, dry, and spongy white pulp, in which the seeds are embedded. Each of the three carpels bears six seeds. Each plant produces 15 to 30 fruits [7,8]



The seeds are gray and 5 millimetres ( $\frac{1}{4}$  in) long by 3 mm ( $\frac{1}{8}$  in) wide. They are similarly bitter, nutty-flavored, and rich in fat and protein. They are eaten whole or used as an oilseed. The oil content of the seeds is 17–19% (w/w), consisting of 67–73% linoleic acid, 10–16% oleic acid, 5–8% stearic acid, and 9–12% palmitic acid. The oil yield is about 400 L/hectare. In addition, the seeds contain a high amount of arginine, tryptophan, and the sulfur-containing amino acids.

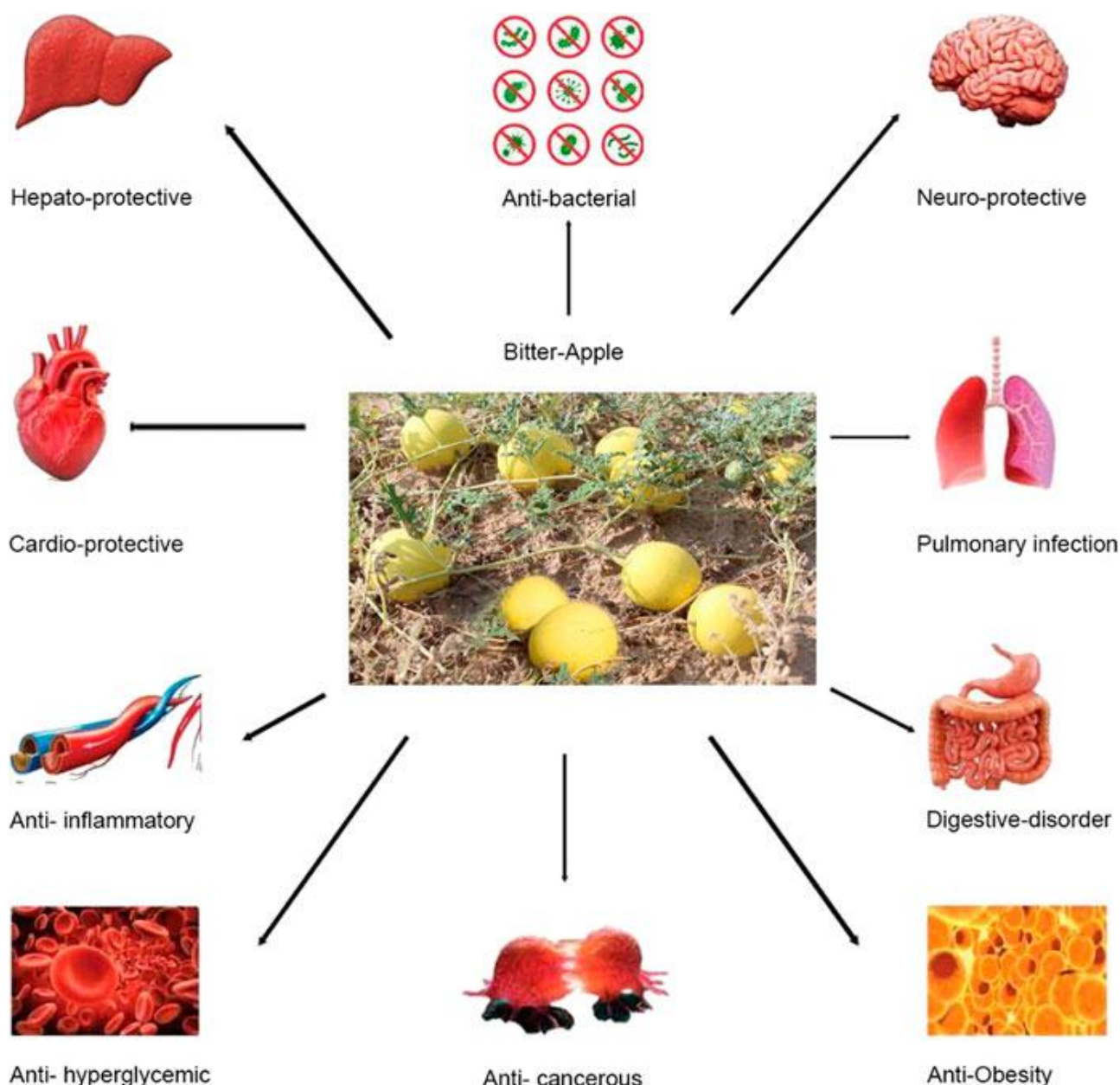




*C. colocynthis*, a perennial plant, can propagate both by generative and vegetative means. However, seed germination is poor due to the extreme xeric conditions, so vegetative propagation is more common and successful in nature. In the Indian arid zone, growth takes place between January and October, but the most favorable period for the vegetative growth is during summer, which coincides with the rainy season. Growth declines as soon as the rains and the temperature decrease and almost stops during the cold and dry months of December and January. [9,10] Colocynth prefers sandy soils and is a good example of good water management which may be useful also on research to better understand how desert plants react to water stress. Cultivated colocynth suffers of climatic stress and diseases such as cucumber mosaic virus, melon mosaic virus, *Fusarium* wilt, etc. as any other crop. To improve it, a relatively new protocol for regeneration has been developed with the aim of incorporating disease and stress resistance to increase yield potential and security avoiding interspecific hybridization barriers

## Results

*C. colocynthis* can be eaten or processed for further uses in medicine and as energy source, e.g. oilseed and biofuel. The characteristic small seed of the colocynth have been found in several early archeological sites in northern Africa and the Near East, specifically at Neolithic Armant, Nagada in Egypt; at sites dating from 3800 BC to Roman times in Libya; and the pre-pottery Neolithic levels of the Nahal Hemar caves in Israel. [11,12]



In Arabia the colocynth had numerous uses in traditional medicine, such as a laxative, diuretic, or for insect bites. The powder of colocynth was sometimes used externally with aloes, unguents, or bandages. Lozenges or troches made of colocynth were called "troches of alhandal" or Trochisci Alhandalæ and used as a laxative. They were usually composed of colocynth, bdellium, and gum tragacanth. Alhandal was a term used in Arabia for the extract of colocynth and is derived from the Arabic الحَنْظَل al-Ḥanẓal, a name for colocynth. The seeds of colocynth, which must be separated from the pulp and heated to make edible, have been used since antiquity as a food source in areas of the Sahara and Sahel where crops frequently fail or regular farming is impossible. The enigmatic early Egyptian ceramic Clayton rings found in the Western Desert may have been portable ovens for roasting colocynth seeds. The desert Bedouin are said to make a type of bread from the ground seeds. The closely related watermelon (*Citrullus lanatus* (Thunb)) was domesticated in Ancient Egypt, and may have been developed for edible seed from cultivated colocynth. [13] In West Africa, some confusion exists between this species and watermelon, whose seeds may be used in much the same way. In particular, the name "egusi" may refer to either or both plants (or more generically to other cucurbits) in their capacity as seed crops, or to a popular soup made from these seeds. The

seed flour is rich in micronutrients, and could therefore be used in food formulations especially in regions with endemic micronutrient deficiencies, such as West Africa. The oil obtained from the seeds (47%) can be used for soap production. The production is not very time- and energy-consuming due to the ability of colocynthis to grow on poor soils with just a little moisture and organic fertilizer. The fruits are harvested still unripe by hand, the rind is removed by peeling and the inner pulp filled with seeds is dried in the sun or in ovens. The seeds yield is about 6.7 to 10 t/ha, which means that for an oil profit of 31 to 47%, oil yields may reach up to 3 t/ha.

Oleic and linoleic acids isolated from *C. colocynthis* petroleum ether extracts show larvicidal activity against mosquitoes[14]

### Conclusions

Bitter apple (*Citrullus colocynthis*) is a perennial herb belonging to kingdom "plantae", division "Magnoliophyta", class "Magnoliopsida", order "Cucurbitales", family "Cucurbitaceae" and genus "*Citrullus*". It is a drought resistance plant that possesses enough potential to bear severe water shortage and known with different names in different regions of the world. *Citrullus colocynthis* is a desert plant that requires arid and sandy soils and is found native to Asia and Mediterranean Basin and also distributed in west coast of North Africa. Seeds of *Citrullus colocynthis* are a rich source of fatty acids such as palmitic acid, stearic acid, oleic acid, linolenic acid and linoleic acid. [15] Some major chemical constituents of *Citrullus colocynthis* are docosan-1- ol acetate, 0,13-dimethyl-pentadec-13-en-1-al, 11,14-dimethyl hexadecane, 14-ol 2-one, 10,14-dimethyl hexadecane 14-ol 2-one, linoleic acid, oleic acid, carbohydrate, amino acid, organic acid, lipid, sterols and phenols. Numerous bioactive compounds are also present in the *Citrullus colocynthis* which are grouped as essential oils along with glycosides, flavonoids, alkaloids, fatty acids and carbohydrates. Due to the presence of various bioactive components, extracts and essential oils of this plant are used to cure ascites, ulcers, tumours, leucoderma, bronchitis, jaundice, asthma, urinary discharges, enlargement of the spleen, tuberculosis glands of neck, dyspepsia, constipation, anaemia, throat diseases and joint's pain elephantiasis.[16]

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